REF AGR11S

AG SARS-Cov-2 Rapid Antigen

A rapid diagnostic test for the detection of SARS-Cov-2 antigen

In vitro **diagnostic medical device**

Intended Use

AG SARS-Cov-2 Rapid Antigen is a fast and convenient immunochromatographic assay for the qualitative detection of SARS-Cov-2 antigen (viral nucleoprotein) from nasal / nasopharyngeal swabs or saliva obtained from patient with signs and symptoms of respiratory infection. The device is designed to support the rapid differential diagnosis of SARS -Cov-2 infection.

This assay is neither intended to screen patients, to be used as auxiliary tool for diagnosis of patients suspected of having SARS-Cov-2 infection, nor to be used for home testing (or self-test). The test result should be confirmed with real-time reverse transcriptase (RT)-PCR diagnostic kit; it does not rule out SARS-Cov-2 infection and should not be used as the sole basis for treatment or other management decisions. This test is for professional and laboratory use.

Introduction

Coronavirus is a single-stranded positive-sense RNA virus with an envelope approximately 80 to 120 nm in diameter. Its genetic material is the largest of all RNA viruses and is an important pathogen of many livestock, pets, and human diseases. It can cause a variety of acute and chronic diseases. Common signs of a person infected with a coronavirus include respiratory symptoms, fever, cough, shortness of breath, and dyspnea. In more severe cases, the infection can lead to pneumonia, severe acute respiratory syndrome, kidney failure, and even death. The 2019 new coronavirus or "SARS-CoV-2", was discovered due to the cases of Wuhan Viral Pneumonia in 2019, and was named by the World Health Organization on January 12, 2020. It can cause colds, the Middle East Respiratory Syndrome (MERS), and more serious diseases such as acuterespiratory syndrome (SARS). This test kit helps with secondary diagnosis of coronavirus infection. The test results are for clinical reference only and should not be used alone as a basis for confirming or excluding cases.

Principle

AG SARS-Cov-2 Rapid Antigen is an antigen-capture immunochromatographic assay that detects the presence of SARS-Cov-2 nucleoprotein in nasal / nasopharyngeal swab samples or saliva. The assay utilizes solid-phase immunoassay techniques following chemical extraction of viral antigens for detection of extracted antigen. The SARS-Cov-2 monoclonal antibodies specific for SARS-Cov-2 antigen are conjugated with colloidal gold, deposited on the conjugate pad, and immobilized on the test zone of the nitrocellulose membrane. When a sample is added, the gold-conjugated antibodies are rehydrated and the SARS-Cov-2 antigen, if present in the sample, will interact with the antibodies.

The antigen-antibody-gold complexes will move to the test region where they will be captured by immobilized antibodies, forming a pink band at the test region indicating a positive result. If the sample does not contain SARS-Cov-2 antigen, no pink band will appear in the test region.

To serve as an internal process control, the control band is designed to indicate that the test was performed properly. By utilizing different antigen-antibody reactions, the control band should always be visible after testing is complete. No pink band at the control region indicates invalid result.

Test Kit Contents (1 test / kit)

Components	Quantity (ea)	Storage
Test Cassette	1	2 to 30 ℃
Reagent Tube	1	
Filter Cap	1	
Instruction for Use		

Kit Storage and Stability

Store the kit at 2 to 30 ℃ (36 to 86 °F) out of direct sunlight. The kit is stable until the expiration date printed on the package box. Do not freeze the kit.

Warning and Precaution

1. Do not reuse test kits.
2. Do not use the kit if the package is damaged or the seal is broken.
3. Do not use extraction buffer tube from other lot.
4. Do not smoke, drink or eat while handling the specimen.
5. Wear personal protective equipment, such as gloves and a lab coat when handling the kit reagents. Wash hands thoroughly after the test.
6. Thoroughly clean spills using a suitable disinfectant.
7. Treat all samples as if they contained an infectious agent.
8. Follow established precautions against microbiological hazards throughout the testing procedure.
9. Dispose of all specimens and materials used to perform the test as biohazardous waste. Laboratory chemical and biohazard wastes must be handled and discarded in accordance with all local, state, and national regulations.

Test Procedure (Saliva)

1. Install the saliva sampling funnel over the reagent tube and spit out the saliva so that the reagent and saliva are mixed.

2. Cap the tube and gently shake it to thoroughly mix the reagent and saliva.

3. With the cap of the tube facing down, drop 5 drops (approximately 120 µl) of the sample into the sample well without air bubbles. (If the viscosity of the sample is too high, it can interfere with diffusion. In that case, use the sample after sufficient dilution.)

4. Read the results after 20 minutes. (Note: DO NOT INTERPRET THE RESULTS AFTER 30 MINUTES OF THE TEST.)

* Specimen Sampling (Swab)

Freshly collected specimens should be processed as soon as possible, but within one hour of sampling. Correct specimen sampling is essential for accurate testing and preparation protocols must be followed. Reagent, specimens and devices must be placed at room temperature (15 to 30 ℃) for test.

Nasopharyngeal Swab

1. Insert a sterile swab into the nostril of the patient until it reaches the surface of the posterior nasopharynx.
2. Swab over the surface of the posterior nasopharynx.
3. Withdraw the swab from the nasal cavity.

Nasal Swab

1. Insert a sterile swab 2 to 3 cm horizontally into the patient's nostril. Rotate the swab 5 times and then leave it on for 5 to 10 secs to absorb any specimen present.
2. Withdraw the swab from the nasal cavity.

* Test Procedure (Swab)

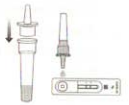
1. Open the seal on the reagent tube.

2. Submerge the swab into the reagent solution contained in the tube.

3. Rotate the swab vigorously and twist it against the side of the tube, at least 10 times.

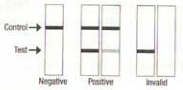
4. Press the side of the tube to get as much liquid as possible from the swab. Dispose of the swab properly.

5. With the cap of the tube facing down, drop 5 drops (approximately 120 µl) of the sample into the sample well without air bubbles. (If the viscosity of the sample is too high, it can interfere with diffusion. In that case, use the sample after sufficient dilution.)



6. Read the results after 20 minutes. (Note: DO NOT INTERPRET THE RESULTS AFTER 30 MINUTES OF THE TEST.)

Interpretation of Test Results



Negative: If a pink band appears only at the control region (C), it indicates that the specimen is negative for SARS-Cov-2.

Positive: If the pink band appears in both the control region (C) and the test region (T), it indicates that the specimen is positive for SARS-Cov-2.

Invalid: If no visible band appears in the control region, retry it with a new test kit. In case the same result appears in repeated tests, please contact your distributor.

Limitation

1. The kit is intended to test saliva or specimens sampled with nasal / nasopharyngeal swab that have NOT been placed in transport media. It is NOT intended to test liquid samples such as wash, aspirated samples or swabs in transport media as excessive dilution may impair results.
2. The kit includes a premade reagent in a ready-to-use unitized tube.
3. Refer to the testing strategy suggested by your local public health authority.
4. Humidity and temperature can negatively affect the results.
5. The kit is to be used for the qualitative detection of SARS-Cov-2 antigen in nasal / nasopharyngeal swab, nasal wash, nasal aspirate or saliva.
6. The test result may be negative if the antigen contained in the sample is below the detection limit of the test.
7. Failure to follow the Specimen Sampling or the Test Procedure may adversely affect test performance and/or invalidate test results.

8. Negative results do not rule out the possibility of infection with non-SARS-Cov-2 pathogens.
9. Positive results do not rule out the possibility of co-infections with non-SARS-Cov-2 pathogens.
10. Positive and negative predictive values are highly dependent on prevalence of COVID-19. False-negative results are more likely to occur when the prevalence of disease is high. On the other hand, false-positive results are more likely to occur when the prevalence is moderate to low.

Performance Characteristic

Clinical Evaluation

A total of 192 nasopharyngeal swab, 48 sputum and 4 nasal swab samples were evaluated.

The specimens were collected from Korea University Guro Hospital and KCDC (2020-051). 60 samples are COVID-19 positive and 138 samples are COVID-19 negative in nasopharyngeal swab. Also, 38 samples are COVID-19 positive and 10 samples are COVID-19 negative in sputum, 2 samples are COVID-19 positive and 2 samples are COVID-19 negative in nasal swab.

AG SARS-Cov-2 Rapid Antigen was compared with a comparator method (Allplex™ 2019-nCoV Assay [RP10243X, RP10244Y]) in clinical sensitivity and clinical specificity tests.

AG SARS-Cov-2 Rapid Antigen showed 97.0% of sensitivity and 99.3% of specificity. The clinical sensitivity and specificity test results of AG SARS-Cov-2 Rapid Antigen are summarized in the table below.

		PCR		
		Positive	Negative	Total
AG SARS-Cov-2 Rapid Antigen	Positive	97	1	98
	Negative	3	149	152
	Total	100	150	250
Sensitivity		97.00% (95% CI : 91.48% to 99.38%)		
Specificity		99.33% (95% CI : 96.34% to 99.98%)		

A total of twelve saliva samples were evaluated.

The specimens were collected from Korea University Guro Hospital. Two samples are COVID-19 positive and ten samples are COVID-19 negative.

AG SARS-Cov-2 Rapid Antigen was compared with a comparator method (Allplex™ 2019-nCoV Assay [RP10243X]) in clinical sensitivity and clinical specificity tests.

AG SARS-CoV-2 Rapid Antigen showed 100% of sensitivity and 100% of specificity. The clinical sensitivity and specificity test results of AG SARS-Cov-2 Rapid Antigen are summarized in the table below.

		PCR		
		Positive	Negative	Total
AG SARS-Cov-2 Rapid Antigen	Positive	2	0	2
	Negative	0	10	10
	Total	2	10	12
Sensitivity		100% (95% CI : 15.81% to 100%)		
Specificity		100% (95% CI : 69.15% to 100%)		

Analytical Sensitivity (Limit of Detection, LOD)

SARS-CoV-2 panel was tested with AG SARS-Cov-2 Rapid Antigen. The LOD concentration was determined by triplicated serial dilution test. The determined LOD concentration was verified with 20 additional replicates. In this study, LOD of AG SARS-Cov-2 Rapid Antigen was determined as 1.6×10^3 $TCID_{50}$/mL.

The results of triplicated ten-fold serial dilution test on the inactivated SARS-CoV-2 strain diluted sample matrix are shown in the table below.

Strain: SARS-Related Coronavirus 2, Isolate USA-WA1/2020, Heat inactivated (VR-1986HK™, Lot#70036071)

Sample Matrix	Virus Serial Dilution Concentration ($TCID_{50}$/mL) (No. of Positive / No. of Replicate)			
	1.6×10^4	1.6×10^3	1.6×10^2	1.6x10
Negative Nasopharyngeal Swab	3/3	3/3	1/3	0/3
Negative Nasal Swab	3/3	3/3	1/3	0/3

Results of a two-fold serial dilution test repeated 20 times at the expected LOD concentration for inactivated SARS-CoV-2 strain diluted sample matrix are shown in the table below.

Strain: SARS-Related Coronavirus 2, Isolate USA-WA1/2020, Heat inactivated (VR-1986HK™, Lot#70036071)

Sample Matrix	Virus Serial Dilution Concentration ($TCID_{50}$/mL) (No. of Positive / No. of Replicate)			
	3.2×10^3	1.6×10^3	8×10^2	4×10^2
Negative Nasopharyngeal Swab	20/20	20/20	11/20	2/20
Negative Nasal Swab	20/20	20/20	13/20	3/20

Analytical Specificity (Cross-Reactivity)

To evaluate the cross-reactivity of AG SARS-Cov-2 Rapid Antigen, the pathogens listed below were tested with 3 lots in triplicate.

The results showed that AG SARS-Cov-2 Rapid Antigen has no significant cross-reactivity with the tested pathogens.

- *Adenovirus1, 7*
- *Enterovirus 71, Tainan/4643/1998*
- *Human coronavirus (OC43, 229E, NL63)*
- *Human metapneumovirus (hMPV)*
- *Influenza A/Michigan/45/2015*
- *Influenza B/Wisconsin/01/2010*
- *MERS-Coronavirus, Irradiated Lysate*
- *Parainfluenza virus type 1,2,3,4*
- *Respiratory syncytial virus Type B*
- *Rhinovirus*
- *SARS-Coronavirus*
- *Pooled human nasal wash*
- *Bodetella pertussis*
- *Candida albicans*
- *Chlamydophila pneumoniae*
- *Haemophilus influenzae*
- *Legionella pneumophila*
- *Mycoplasma pneumoniae*
- *Streptococcus pneumoniae*
- *Streptococcus pyogenes, Group A*

Analytical Specificity (Interference)

To test the possible effects of interfering substances, AG SARS-Cov-2 Rapid Antigen was tested in triplicate using specimen spiked with the following substances. (acetaminophen 10mg/mL, acetylsalicylic acid 15mg/mL, beclomethasone 0.5mg/mL, chlorpheniramine maleate 5mg/mL, dextromethorphan HBr 2mg/mL, diphenhydramine HCl 5mg/mL, ephedrine HCl 10mg/mL, guaialcol glyceryl ether 20mg/mL, histamine dihydrochloride 10mg/mL, mometasone 1mg/mL, mucin 2%, throat drop (Halls) 15%, throat drop (Ricola) 15%, throat drop (Zinc) 15%, nasal spray (Afrin) 15%, nasal spray (VicksSinex) 15%, nasal spray (Zicam) 15%, oxymetazoline HCl 10mg/mL, phenylephrine HCl 50mg/mL, phenylpropanolamine 20mg/mL, tobramycin 1mg/mL, triamcinolone 1mg/mL, whole blood 5%)

Hook Effect

High concentration samples were tested with AG SARS-Cov -2 Rapid Antigen. No hook effect was observed. All the samples were tested in triplicate with concentrations from 1.6×10^6 to 1.6×10^3 $TCID_{50}$/mL as well as negative samples. The result indicates no hook effect.

Stability (Acceleration Test)

Accelerated stability test for 7 weeks showed the same performance on all samples and confirmed that they had a shelf life of 12 months. The test is still in progress and stability can be extended based on the results of subsequent tests.

References

1. Clinical management of severe acute respiratory infection (SARI) when COVID-19 disease is suspected. *Interim guidance. World Health Organization. 13 March 2020*
2. Report of the WHO-China Joint Mission on Coronavirus Disease 2019 (COVID-19). *World Health Organization. 16~24 February 2020*
3. The Epidemiological Characteristics of an Outbreak of 2019 Novel Coronavirus Diseases (COVID-19). *Chinese Center for Disease Control and Prevention. CCDC Weekly, 2(8):113-122, 2020*
4. A novel coronavirus outbreak of global health concern. *Wang C et al. Lancet, 395(10223):470-473, 2020*

Description of Symbols Used

Symbol	Description	Symbol	Description
REF	Catalogue number		Caution
LOT	Batch code		Manufacturer
	Use-by date		Consult instructions for use
	Upper limit of temperature		

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